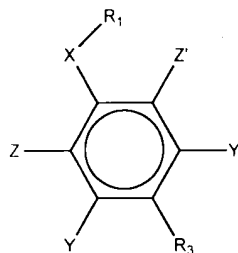


8. A method of inhibiting picornavirus activity, comprising contacting the picornavirus with a compound of the formula:



wherein

X is selected from the group consisting of C=O, S=O, C=S, (C=O)-NH, (C=O)-O and (C=O)-S:

R₁ is selected from the group consisting of:

(i) hydrogen or a hydrocarbon chain from 1 to about 10 carbons long selected from the group consisting of saturated, unsaturated and fluorinated, wherein said hydrocarbon chain is unsubstituted or substituted with at least one R¹¹, wherein R¹¹ is selected from the group consisting of:

(ia) C₁-C₄ alkyl, C₂-C₄ alkenyl, C₃-C₈ cycloalkyl, C₆-C₁₀ bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamylloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) NR¹³R¹⁴, CO₂R¹³, O(C=OR¹³), SO₂R¹⁴, SOR¹⁴, (C=O)NR¹³R¹⁴, or NR¹⁴(C=O)R¹³;

wherein:

R¹³ is selected from the group consisting of hydrogen, phenyl, benzyl, C₁-C₆ alkyl and C₃-C₆ alkoxyalkyl; and

R¹⁴ is selected from the group consisting of hydrogen, hydroxyl, and benzyl;

(ii) an oligopeptide or peptidomimetic molecule of 1 to 5 amino acids;

(iii) C₃-C₆ cycloalkyl, C₆-C₁₀ bicycloalkyl, C₃-C₇ cycloalkylmethyl, or C₇-C₁₀ arylalkyl, which may be additionally substituted with R¹¹ as defined above;

R₃ is selected from the group consisting of:

(i) hydrogen, phenyl, hydroxyl, C₁-C₁₂ hydrocarbon chain or O-C₁-C₁₂ hydrocarbon chain which may be additionally substituted with at least one R¹¹ as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydroxyl, sulfhydryl, carboxyl and NHR¹¹, wherein R¹¹ is defined as above;

Z' is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy or halogen;

(ii) hydrogen; and

(iii) C₁-C₄ alkyl, C₂-C₄ alkenyl, C₃-C₇ cycloalkenyl, or C₁-C₃ alkoxy which may be additionally substituted with at least one R¹¹ as defined above;

alternatively Z' and R₁ collectively form a ring system selected from the group consisting of:

(a) C₅-C₈ carbocyclic ring which may be saturated or unsaturated, and which may be additionally substituted with at least one R¹¹ as defined above; and

(b) C₅-C₁₀ heterocyclic ring system which may be saturated or unsaturated and which includes at least one nitrogen, oxygen or sulfur atom, and which may be additionally substituted with at least one R¹¹ as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydrogen, halogen, C₁-C₄ haloalkyl, or C₁-C₄ haloalkoxy;

(ii) carbamyl, carbamido, cyano, COR¹¹, vinyl, nitro, SO₂R¹¹, or SOR¹¹, wherein R¹¹ is defined above;

(iii) C₁-C₃ alkyl which may be additionally substituted with at least one R¹¹ as defined above; and

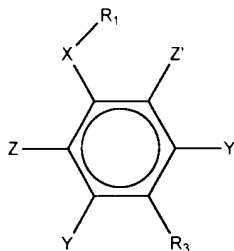
(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R₁ is a fluorinated keto acyl, Z is hydrogen;

for a time and under conditions effective to inhibit replication of said picornavirus.

12. A method according to claim 8, wherein said picornavirus is a rhinovirus.

17. A method of inhibiting picornavirus activity, comprising contacting the picornavirus with a compound of the formula:



wherein X is selected from the group consisting of $-C=O-$, $-S=O-$, and $-C=S-$;

R_1 is selected from the group consisting of:

(i) a hydrocarbon chain which may be unsubstituted or substituted with at least one R^{11} , wherein R^{11} is selected from the group consisting of:

(ia) C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_3 - C_8 cycloalkyl, C_6 - C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, COR^{13} , $O(C=OR^{13})$, SO_2R^{14} , SOR^{14} , $(C=O)NR^{13}R^{14}$, or $NR^{14}(C=O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1 - C_6 alkyl, and C_3 - C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, and benzyl;

R_3 is selected from the group consisting of:

(i) phenyl, hydroxyl, C_1 - C_{12} hydrocarbon chain and $O-C_1$ - C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide or a peptidomimetic molecule of 1 to 3 amino acids, joined to the backbone by an oxygen;

Z is selected from the group consisting of hydroxyl, sulfhydryl, carboxyl, and NHR^{11} , wherein R^{11} is defined as above;

Z' is selected from the group consisting of:

- (i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy, and halogen;
- (ii) C₁-C₄ alkyl, C₂-C₄ alkenyl, C₃-C₇ cycloalkenyl and C₁-C₃ alkoxy which may be additionally substituted with at least one R¹¹ as defined above;

Y and Y' are independently selected from the group consisting of:

- (i) hydrogen, halogen, C₁-C₄ haloalkyl, or C₁-C₄ haloalkoxy;
- (ii) carbamyl, carbamido, cyano, COR¹¹, vinyl, nitro, SO₂R¹¹, or SOR¹¹ wherein R¹¹ is defined above;

R¹¹ is defined above;

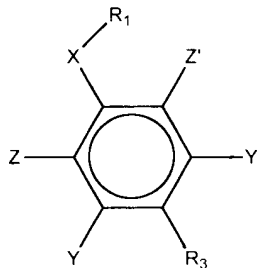
(iii) C₁-C₃ alkyl which may be additionally substituted with at least one R¹¹ as defined above; and

- (iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R₁ is a fluorinated keto acyl, Z is hydrogen

for a time and under conditions effective to inhibit replication of said picornavirus.

19. A method of inhibiting picornavirus activity, comprising contacting the picornavirus with a compound of the formula:



wherein X is selected from the group consisting of -C=O-, -S=O-, and -C=S-;

R₁ is selected from the group consisting of:

(i) a hydrocarbon chain which may be unsubstituted or substituted with at least one R¹¹, wherein R¹¹ is selected from the group consisting of:

- (ia) C₁-C₄ alkyl, C₂-C₄ alkenyl, C₃-C₈ cycloalkyl, C₆-C₁₀ bicycloalkyl or aryl which may be substituted or unsubstituted;
- (ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;
- (ic) an oligopeptide of 1-3 amino acid residues; and

(id) $\text{NR}^{13}\text{R}^{14}$, COR^{13} , $\text{O}(\text{C}=\text{OR}^{13})$, SO_2R^{14} , SOR^{14} , $(\text{C}=\text{O})\text{NR}^{13}\text{R}^{14}$,
or $\text{NR}^{14}(\text{C}=\text{O})\text{R}^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1 - C_6 alkyl, and C_3 - C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, and benzyl;

R_3 is selected from the group consisting of:

(i) phenyl, hydroxyl, C_1 - C_{12} hydrocarbon chain and $\text{O}-\text{C}_1$ - C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids[, an oligopeptide of 1 to 3 amino acids] joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydroxyl, sulfhydryl, carboxyl, and NHR^{11} , wherein R^{11} is defined as above;

Z' is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy, and halogen;
(ii) C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_3 - C_7 cycloalkenyl and C_1 - C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydrogen, halogen, C_1 - C_4 haloalkyl, or C_1 - C_4 haloalkoxy;
(ii) carbamyl, carbamido, cyano, COR^{11} , vinyl, nitro, SO_2R^{11} , or SOR^{11} wherein

R^{11} is defined above;

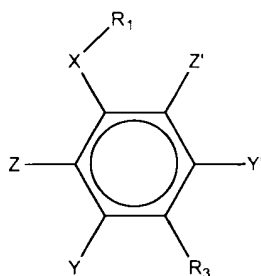
(iii) C_1 - C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; and

(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids;

and pharmaceutically acceptable salts thereof; with the proviso that when $\text{X}-\text{R}_1$ is a fluorinated keto acyl, Z is hydrogen;

for a time and under conditions effective to inhibit replication of said picornavirus.

20. A method of inhibiting picornavirus activity, comprising contacting the picornavirus with a compound of the formula:



wherein

X is selected from the group consisting of C=O, S=O, C=S, (C=O)-NH, (C=O)-O and (C=O)-S:

R₁ is selected from the group consisting of:

(i) hydrogen or a hydrocarbon chain from 1 to about 10 carbons long selected from the group consisting of saturated, unsaturated and fluorinated, wherein said hydrocarbon chain is unsubstituted or substituted with at least one R¹¹, wherein R¹¹ is selected from the group consisting of:

(ia) C₁-C₄ alkyl, C₂-C₄ alkenyl, C₃-C₈ cycloalkyl, C₆-C₁₀ bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) NR¹³R¹⁴, CO₂R¹³, O(C=OR¹³), SO₂R¹⁴, SOR¹⁴, (C=O)NR¹³R¹⁴, or NR¹⁴(C=O)R¹³;

wherein:

R¹³ is selected from the group consisting of hydrogen, phenyl, benzyl, C₁-C₆ alkyl and C₃-C₆ alkoxyalkyl; and

R¹⁴ is selected from the group consisting of hydrogen, hydroxyl, and benzyl;

(ii) an oligopeptide or peptidomimetic molecule of 1 to 5 amino acids;

(iii) C₃-C₆ cycloalkyl, C₆-C₁₀ bicycloalkyl, C₃-C₇ cycloalkylmethyl, or C₇-C₁₀ arylalkyl, which may be additionally substituted with R¹¹ as defined above;

R₃ is selected from the group consisting of:

(i) hydrogen, phenyl, hydroxyl, C₁-C₁₂ hydrocarbon chain or O-C₁-C₁₂ hydrocarbon chain which may be additionally substituted with at least one R¹¹ as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids joined to the backbone by an oxygen or a peptidomimetic;

Z is OH;

Z' is H;

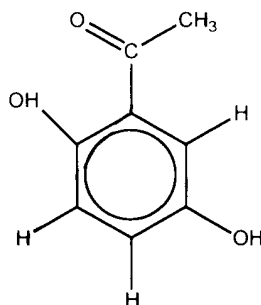
Y is H;

Y' is OH;

and pharmaceutically acceptable salts thereof;

for a time and under conditions effective to inhibit replication of said picornavirus.

21. A method of inhibiting picornavirus activity, comprising contacting the picornavirus with a compound of the formula:



and pharmaceutically acceptable salts thereof for a time and under conditions effective to inhibit replication of said picornavirus.